In case 1, electrocardiograms (Figure 1) showed significant interval changes, which were assumed (incorrectly) to be consistent with anterolateral infarction. In fact, the patient had atrial fibrillation (no P waves), transient right bundle branch block, clockwise rotation, anterior Q waves and a mild vertical plane axis shift, all consistent with massive pulmonary embolism. This patient showed an uncommon pattern of pseudoinfarction associated with massive pulmonary embolization described above. It should be emphasized that the original interpretation was not correct and that other possible explanations for the changes should have been entertained.

The electrocardiogram in case 2 (Figure 2) is an example of right ventricular strain (systolic overload) due to pulmonary embolism. Anterior and right precordial ST-segment elevation was misinterpreted as right ventricular ischemia/infarction and, consequently, pulmonary embolism was not considered.

In conclusion, we have presented two cases of massive pulmonary embolism simulating myocardial infarction and left ventricular dysfunction. Hemodynamic and electrocardiographic changes mimicking myocardial infarction obscured the correct diagnosis. These cases underscore the protean clinical manifestations of pulmonary embolization and reinforce the fact that scrutiny of all available data with special attention to clinical and electrocardiographic inconsistencies is critical for the correct diagnosis and appropriate therapy for this deadly masquerader.

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Atenolol Overdosage in a Patient With Progressive Renal Failure

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ATENOLOL (Tenormin, Stuart) is a relatively new, synthetic, β-selective adrenoreceptor-blocking agent. In contrast to most of the other drugs of its class, such as propranolol, which are relatively fat soluble and are primarily metabolized in the liver, atenolol is water soluble and is excreted by the kidney. Dosage reduction is therefore required when using atenolol in treating patients who have renal insufficiency.[1]

We report a case of atenolol overdosage due to renal failure that was successfully treated with continuous isoproterenol infusion.

Report of a Case

The patient, a 48-year-old man, had been in good health until six months before admission, at which time he noted the gradual onset of bilateral lower extremity paresthesia. Two months before admission, he was seen at another facility for gross hematuria. An intravenous ureterogram was normal and the patient underwent a three-week course of prednisone, 20 mg per day, which resulted in resolution of the hematuria.

(Giang DW, Isaeff DM: Atenolol overdosage in a patient with progressive renal failure. West J Med 1986 Jul; 145:101-103)

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The patient presented to the emergency department of another facility 18 days before admission complaining of the sudden onset of palpitations, chest pain, dyspnea and malaise. Cardiac monitoring documented atrial fibrillation with a ventricular response rate of 130 beats per minute. A total of 8 mg of verapamil was administered intravenously over 15 minutes, resulting in conversion to sinus rhythm at 80 beats per minute. On physical examination, no abnormalities were noted. Admission laboratory studies elicited the following values: blood urea nitrogen 43 mg per dl, creatinine 3.0 mg per dl, total protein 5.5 mg per dl and albumin 3.1 mg per dl. A urinalysis showed a specific gravity of 1.016, proteinuria (3+), hematuria (4+) and a sediment consisting of four to eight leukocytes, many erythrocytes, moderate amount of bacteria and zero to one casts (unspecified type). A myocardial infarction was ruled out by serial electrocardiograms and cardiac enzymes. Another intravenous ureterogram was normal. The Westergren sedimentation rate was 51 mm per hour. Results of further serologic and urine testing were nonspecific. The patient was given ampicillin, 500 mg every six hours orally, for the urinary tract infection; furosemide, 40 mg a day, and atenolol, 50 mg a day. He remained in normal sinus rhythm with a normal blood pressure.

On discharge and eight days before admission to our facility, the patient had a urea nitrogen level of 79 mg per dl and a creatinine level of 3.9 mg per dl. A regimen of atenolol, 50 mg a day, furosemide, 40 mg a day, and temazepam, 30 mg at bedtime, was dispensed.

The patient arranged to be admitted to Loma Linda University Medical Center for a second opinion concerning his renal problems. He continued to comply with his medication regimen. On the day before admission, the patient had two syncopal episodes on arising. Each lasted less than a minute, and they were not associated with chest pain, palpitations, aura, abnormal movements or a postictal state. By the day of admission, he could not even sit up in the car without orthostatic light-headedness.

On initial evaluation, the patient was found to have an apical pulse rate of 20 beats per minute and a blood pressure of 74/28 torr supine. The patient lost consciousness upon attempting to sit up in bed. He was placed in the Trendelenburg position and transported to the intensive coronary care unit, where cardiac monitoring showed complete heart block with a ventricular rate of 12 per minute (see Figure 1).

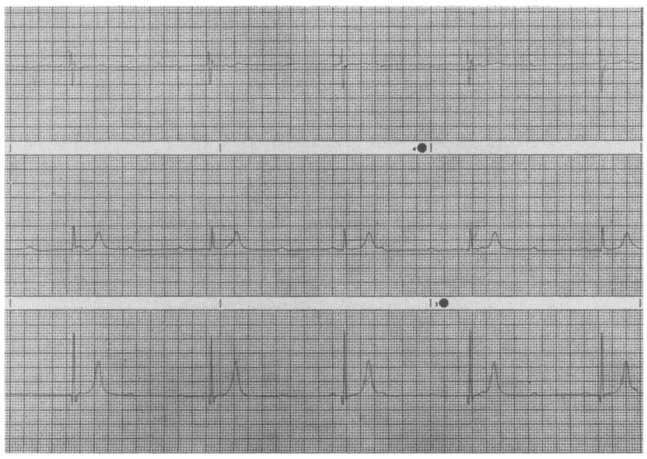

Figure 1.—Electrocardiographic rhythm strips taken at time of admission to the coronary care unit.

On physical examination he was noted to be diaphoretic and lethargic but responded to voice and was well oriented. No carotid bruits were heard. The lungs had fine bibasilar rales but no wheezing. Heart sounds were distant. There was a regular bradycardia with rare extra beats. There were no murmurs on auscultation. The abdomen showed no abnormalities and no organomegaly. The extremities were warm with weak pulses but without edema. There was no presacral edema.

Initially atropine sulfate was administered by intravenous bolus (a total of 1 mg over three minutes) without response. An intravenous infusion of isoproterenol hydrochloride (2 mg diluted in 250 ml of 5% dextrose solution) was begun at a rate of 3.3 μg per minute. The infusion rate was titrated upward rapidly until a clinical effect was noted with an infusion rate of 6.7 μg per minute. Eight minutes after initiating the isoproterenol infusion, the pulse was 46 per minute and the blood pressure was 104/20 torr. Intra-arterial peripheral blood pressure monitoring was instituted.

Laboratory studies done at admission (before treatment) elicited the following values: sodium 128, potassium 5.8, chloride 93 and carbon dixoide 21 mEq per liter; blood urea nitrogen 119, creatinine 6.9, total protein 5.1 and albumin 2.5 mg per dl; alkaline phosphatase 80, aspartate aminotransferase (formerly glutamic-oxaloacetic transaminase) 27 and alanine aminotransferase (formerly glutamic-pyruvic transaminase) 13 units per liter; lactate dehydrogenase 179 units per ml; calcium 2.0 mmol per liter, and phosphorus 2.9 mg per dl. The Westergren sedimentation rate was 121 mm per hour, the leukocyte count was 11,700 per μl with 82% segmented neutrophils, hemoglobin 9.2 grams per dl, hematocrit 27.4% with normochromic and normocytic indices and platelet count 332,000 per μl. Arterial blood gas measurements with the patient receiving 4 liters of oxygen per minute via nasal cannula showed a pH of 7.43, a partial carbon dioxide pressure of 29 torr, a partial oxygen pressure of 98 torr and bicarbonate 19 mEq per liter.

During the first four days in hospital, the patient was treated with an intravenous infusion of isoproterenol that was titrated to keep the mean arterial blood pressure above 60 torr. Infusion rates up to 8.7 μg per minute were necessary. He had no further syncopal episodes. Cardiac monitoring revealed variable second- and third-degree blocks. Temporary pacing was not required to maintain a satisfactory pulse rate and arterial pressure. Potassium-binding resin was administered to decrease the serum potassium level. The urea nitrogen and creatinine values improved without the use of dialytic therapy.

By the fourth hospital day, the patient had a pulse of 85 per minute and a blood pressure of 86/43 torr, and the isoproterenol dosage was tapered off. At that time, the urea nitrogen level was 93 mg per dl, the creatinine level was 3.9 mg per dl and the potassium value was 4.7 mEq per liter. Over the following two days, the patient had alternating atrial fibrillation and atrial flutter with ventricular response rates varying between 60 and 128 per minute. Digoxin was administered intravenously to control a rapid ventricular response and the patient converted to normal sinus rhythm on the seventh hospital day while undergoing a muscle biopsy under local anes-

thesia. At that time the urea nitrogen level was 65 mg per dl and the creatinine 2.8 mg per dl.

The patient's condition remained stable throughout the rest of the hospital stay. A 24-hour continuous electrocardiographic monitor on the 12th hospital day showed a normal sinus rhythm with a rate ranging between 72 and 110. An echocardiogram showed mild left atrial and left ventricular dilatation and normal left ventricular function. A percutaneous needle biopsy of the kidney showed crescentic glomerulonephritis. Prednisone therapy, 120 mg per day, was started, followed by a tapering regimen. After 33 days in hospital, the patient was discharged on a regimen of prednisone and hydrochlorothiazide. At discharge, the urea nitrogen level was 20 mg per dl and creatinine 1.8 mg per dl. Since discharge (18 months), the patient has remained asymptomatic, with a creatinine level of 1.5 mg per dl.

Discussion

A previous case of atenolol overdosage has been reported that involved the ingestion of 1,200 mg of atenolol during an attempted suicide by a 24-year-old woman under treatment for hypertension. The patient's pulse remained above 60 per minute and her blood pressure remained hypertensive. She was treated conservatively and no complications developed.[2] Another case was reported of a suicide attempt of a 22-year-old woman ingesting 1,000 mg of atenolol. The only electrocardiographic abnormality noted was frequent sinus pauses persisting for 34 hours postingestion but progressively decreasing in frequency during observation.[3]

In 1979 Frishman and co-workers reviewed the world literature on overdoses of β-adrenoreceptor-blocking agents. In all, 22 cases were reviewed. Bradycardia, hypotension, low cardiac output, cardiac failure and cardiogenic shock were reported as common complications. Bronchospasm, respiratory failure, seizures, hypoglycemia and eventual asystole were also reported. Atropine, 0.5 to 3.0 mg administered intravenously, was recommended as initial therapy, to be followed by isoproterenol infusion if atropine was not successful. Dobutamine and norepinephrine were also used. In a case wherein medical management fails to reverse bradycardia, a temporary pacemaker is required.[4]

In Frishman's second edition of *Clinical Pharmacology of the β-Adrenoceptor Blocking Drugs,* he has updated treatment that suggests the use of a selective β-adrenoreceptor agonist in treating overdosage with β_1-selective adrenoreceptor blocking agents.[5]

Other treatment modalities have been suggested for cases refractory to isoproterenol, including intravenous administration of glucagon[6] and calcium chloride.[7]

The patient in the case described here showed severe bradycardia and hypotension due to impaired renal clearance of atenolol and consequent excessive β-adrenoreceptor blockage. Indeed, atenolol may have exacerbated the renal failure by decreasing renal perfusion in this case.

Although no levels of atenolol were assayed, the constellation of symptoms suggests atenolol overdosage as the most likely cause. Neither temazepam nor furosemide have been reported to cause bradycardia, although both are known to cause hypotension and other symptoms reported by the patient.[8]

The patient did not manifest bronchospasm, although isoproterenol would tend to counteract this symptom. At no point was there evidence of congestive heart failure other than the slight bibasilar rales on admission. The patient responded dramatically to isoproterenol infusion but did not respond to intravenous administration of atropine. A temporary pacemaker was not required.

β-Adrenoreceptor-blocking agents are deactivated by the liver or kidney depending on their degree of water solubility. Propranolol, metoprolol tartrate, labetalol hydrochloride and timolol maleate are all relatively lipid soluble and are primarily metabolized in the liver. Contrariwise, atenolol and nadolol are relatively water soluble and are excreted by the kidney. Pindolol is intermediate.[9]

To avoid toxicity in the presence of impaired renal function, the manufacturer recommends reducing the dosage of atenolol according to the creatinine clearance: clearances greater than 35 ml per minute per 1.73 m^2 do not require adjustment; for clearances between 15 and 35 ml per minute per 1.73 m^2, 25 mg per day (or 50 mg every other day) is recommended.[10]

Although dosage reduction can be used to guide atenolol administration in patients with stable renal function, it seems prudent to substitute a lipid-soluble agent in patients whose renal state is changing rapidly and in whom β-adrenoreceptor blockage is required.

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